REJECTION UNDER 35 U.S.C. § 103

The Examiner rejected Claims 184-187 under 35 U.S.C. §103 as being unpatentable over Drucker (USP 5846937) in view of Galloway (USP 5705483); or Smith (USP 5908830) in view of Galloway; or Knudsen (WO 98/20895) in view of Galloway; or Gelfand (EP 0619322) in view of Galloway; or Kirk (WO 93/18785) in view of Galloway.

Applicants assert that the Examiner has not made a *prima facie* case of obviousness. The cited references fail to provide any teaching, suggestion or motivation to those skilled in the art to administer specific GLP-1 analogs by pulmonary means. Motivation is a factual question that cannot be resolved on "subjective belief and unknown authority." *In re Lee,* 277 F.3d 1338, 1344 (Fed. Cir. 2002). "It is improper, in determining whether a person of ordinary skill would have been led to this combination of references, simply to '[use] that which the inventor taught against its teacher.'" *Id.*

Further, implicit in the Examiner's argument is the use of Applicant's specification to support the prior arts assertion of efficacy. The Federal Circuit has also in several cases stated that hindsight is not a justifiable basis on which to find an invention obvious. *See In re Dembiczak,* 175 F.3d 994 (Fed. Cir. 1999).

> Measuring a claimed invention against the standard established by section 103 requires the oft-difficult but critical step of casting the mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then-accepted wisdom in the field.

Id. at 999. Thus, to avoid a hindsight analysis wherein the inventor's teachings are used against him, "there must be a rigorous application of the requirement for showing the teaching or motivation to combine the prior art references." *Id.* Without using Applicant's specification, there is no teaching, or motivation to combine the references and arrive at the successful pulmonary administration of specific GLP-1 analogs.

Additionally, the cited references (Drucker, Smith, Knudsen, Gelfand, or Kirk) either by themselves or with the Galloway reference do not establish a reasonable likelihood that any GLP-1 peptide could be expected to be administered by pulmonary means. The Examiner previously expressed doubt as to whether intact and active GLP-1 peptides appear

in the serum. Thus, the Examiner suggested that the cited references do not provide a reasonable expectation of success. This is due to primarily to the unpredictability generally associated with pulmonary delivery. Now the Examiner is saying that the references assertion of efficacy is enough. The references cited by the Examiner not only fail to suggest anything with respect to the specific GLP-1 analogs claimed in the present application, but also do not make it possible to predict whether the specific GLP-1 analogs of the present invention could be administered by pulmonary means and would be beneficial in lowering blood glucose. Courts have characterized inventions like the present one as unpredictable because a degree of trial and error is normally required before one can know whether a given strategy will succeed. *See e.g., Ex parte Hitzeman,* 9 U.S.P.Q.2d 1821, 1823 (Bd. Pat. App. & Int. 1988) ("case involves highly unpredictable factors including unique, delicate, and unpredictable biochemical and genetic actions"). However, Applicants have shown: 1) a GLP-1 molecule can be administered by pulmonary means; 2) the GLP-1 molecule is absorbed into the blood, and; 3) the GLP-1 molecule can lower plasma glucose. None of the references, alone or in combination, cited by the Examiner have demonstrated any of these properties.

The references cited by the Examiner disclose merely the statement that GLP-1 molecules can be administered by pulmonary means. There is no support in the references for such a broad statement. The court noted in *In re Baird,* 16 F.3d 380, 382 (Fed. Cir. 1994), "the fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious." The prior art generic formula in *Baird* encompassed numerous variables, and the court found the selected compounds patentable over the genus because there was nothing to suggest that one should select the variables that resulted in the selected compounds. *Id.* In the present case, Applicants have selected specific GLP-1 analogs that can be administered by pulmonary means over a boilerplate assertion that any GLP-1 compound can be administered by pulmonary means. Thus, a case of obviousness cannot be supported. The references cited by the Examiner do not explicitly or implicitly teach, suggest, or motive the present invention with any expectation of success.

Additionally, the Examiner suggests that Applicants are implicitly arguing "that administration of pharmacologically active intact peptide to the blood via the lung will occur regardless of whether the peptide that is administered contains e.g., 5 amino acids, or 500

amino acids. It is implicitly argued that any peptide regardless of sequence or composition will be effective in this regard." This, however, is simply not true. The specific GLP-1 analogs have a backbone structure from which one additional amino acid may be substituted. Further, the structure is tied to a function of having to lower plasma glucose. Therefore, the Examiner's assertion that administration of pharmacologically active intact peptide to the blood via the lung will occur regardless the peptide used is logically incorrect. The genus sought to be claimed by the Applicants is within the scope of the invention and should be granted such protection.

The Examiner also rejected Claims 184-190, 193, and 194 under 35 U.S.C. §103 as being unpatentable over Drucker (USP 5846937) in view of Galloway (USP 5705483). The Examiner stated that the reference provides an affimative recitation that pulmonary administration of the peptide in the form of an aerosol spray in a metered amount would lead a medical practitioner to know how to achieve pulmonary administration. Again, the Examiner is being inconsistent with this argument. Previously, the Examiner would not consider the prior art when making an enablement rejection, but now is selectively using the it to support an obviousness rejection. This type of inconsistency is inappropriate. *See Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367 (Fed. Cir. 1986). The references cited by the Examiner to support a case for obviousness do not provide any expectation that pulmonary delivery would be successful in providing sufficient bioavailability to be therapeutically effective. Applicants respectfully submit that the Examiner withdrawal this rejection.

SUMMARY AND CONCLUSION

Applicants respectfully assert that the application is now in condition for allowance. Applicants claim to pulmonary administration of specific GLP-1 analogs are not taught or suggested by the cited references. It is not unreasonable to allow Applicants to broaden the scope of the allowed claims to match the technical contribution to the art by allowing one additional amino acid substitution. If, for any reason, the Examiner feels that a telephone conversation would be helpful in expediting the prosecution of this case, the Examiner is urged to call me.

Respectfully submitted,

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